BONE CEMENT AND GENTAMICIN IN THE TREATMENT OF BONE INFECTION. BACKGROUND AND IN VITRO STUDY

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ABSTRACT
Objective: To determine the elution characteristics of the antibiotic (gentamicin) mixed with bone cement. Methods: 480mg of gentamicin was added to 40g of bone cement. Ten specimens were immersed in buffered saline solution for 28 days. Samples of days 1, 2, 7, 14, 21 and 28 were analyzed by the fluorescence polarization immunoassay method. Results: Most of the gentamicin was eluted from the cement in the first 24 hours. A gradual downslide occurred between days 2 and 14. By the 28th day, there was no trace of the antibiotic. Conclusion: The mixture released high amounts of the antibiotic in a predictable (therapeutic) manner during at least fourteen days.

Keywords: Infection, Osteomyelitis. Polymethylmethacrylate. Gentamicin.
ture, humidity and pressure, affecting their physical characteristics. The type of antibiotic, the quantity added and the exchange of fluids in the wound also influence them. The three-dimensional form is of great importance, whereas the maximum elution is obtained when using small elongated beads, which provide a larger surface area. The addition of antibiotic alters the mechanical properties of the cement and liquid gentamicin, in the dose of 480mg, decreases the compression resistance by 49% and traction resistance by 46%. The release of the antibiotic by PMMA can be qualified as bimodal. In the first hour it is quickly dispersed, presumably by dissolution on the exposed surface of the cement. After this period, there is much slower release, by means of passive diffusion through the cement mass. In this typical biphasic pattern, a peak occurs in the first 24 hours, followed by a long period of release of low doses, which can last from days to months, with traces of the antibiotic still being found 5 years after implantation.

The antibiotic should preferably be in powdered form, as the aqueous solution has limited incorporation. The agent should be stable at high temperatures, as the interior of the cement mass can reach 107 °C during polymerization. It should also present a low risk of allergic reactions. The quantity of antibiotic released depends on its concentration in the mixture and on the quantity of mixture implanted in the patient, whereas the doses recommended for clinical use in infection treatment are: from 2 to 3g for gentamicin, 3g for tobramycin, 4g for vancomycin, cefepime and imipenem, and 6g for cefazolin and nafcillin, for a packet of 40g of bone cement.

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Gentamicin has been the antibiotic most frequently used for local application and its mixture with PMMA is commercially available in Brazil at a low price, and its addition to PMMA at the time of use might be a form of reducing costs and of facilitating access to this therapeutic method. The aim of this study was to analyze in vitro the elution characteristics of gentamicin added to bone cement at the time of use, with the intention of evaluating safety for clinical use of this mixture.

MATERIAL AND METHODS

Making of test specimens

A Teflon resin® mold was developed for the preparation of the test specimens, with holes measuring 15mm in depth and 6mm in diameter and a second hole at the center measuring 3mm in depth and 3mm in diameter, which reached the other side. (Figure 1) The bone cement used was Surgical Simplex P® (Howmedica, Limerick, Ireland). The preparation was performed at room temperature under aseptic technique. The polymer was placed in a tub with 480mg of powdered gentamicin sulfate, and mixed with 40g of polymer until a homogeneous mixture was formed, at which point the monomer (liquid) was added. After this the mixture was introduced manually in the mold. (Figure 2) The surplus was removed with a spatula and the cement left to cure for thirty minutes, before the removal of the test specimens.
DISCUSSION

Serum peaks that range from 5 to 8μg/ml are achieved with the parenteral administration of gentamicin in the recommended standard dose (1.5mg/Kg every 8 hours), yet experimental studies estimated that concentrations in the bone tissue are below 1μg/ml.23,24 Seldes et al.16 performed an in vitro evaluation of the addition of 480mg of liquid gentamicin to Palacos R®, using cylindrical test specimens with an area of 282.6mm². Average levels of 26.4μg/ml were reached in the first 24 hours, falling to 4.15μg/ml at three weeks.

In this study with the addition of 480mg of powdered gentamicin to Simplex® and the making of test specimens with an area of 367mm², the participants obtained concentrations of 6.15μg/ml in the first 24 hours, dropping to 0.06 μg/ml in the third week. This difference can be explained by the variations in the experiment conditions and by the fact that the Simplex® cement has a performance inferior to Palacos® for gentamicin elution.20

Based on the outcome of this study, the use of 480mg of gentamicin was capable of dispersing quantities above 1μg up to the 14th day. Higher concentrations over a longer period of time should be expected in increasing the quantity of antibiotic added to the cement and the quantity of the mixture used.

CONCLUSION

The mixing of 480mg of powdered gentamicin with a 40g packet of acrylic cement presented predictable elution properties, maintaining therapeutic levels of antibiotic up to the second week, thus serving as an alternative to prepare for the expansion of local antibiotic use in the treatment and in the prophylaxis of bone infection.

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REFERENCES